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A Record of the Progress of Pharmacy and the Allied Sciences

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Vol. 103 **SEPTEMBER, 1931** **No. 9**

CONTENTS

Editorials:

Pharmaceutical Discoveries 489

The Druggist Himself 492

Original Articles:

A Study of Rhubarb and a Quantitative Determination of Some of Its Constituents. By Peter Valaer, Washington, D. C. 495

More About Syrup of Ferrous Iodide. By H. V. Arny and A. Steinberg, New York, N. Y. 504

Who Is to Dispense Hypodermic and Intravenous Medications. By Louis Gershenfeld, Philadelphia, Pa. 509

The Pharmacist's Show Globes. By Aaron Lichtin, Philadelphia, Pa. 515

Report of Committee on Drug Market to the Pennsylvania Pharmaceutical Association, 1931 522

Medical and Pharmaceutical Notes 529

Book Reviews 538

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THE AMERICAN
JOURNAL OF PHARMACY

VOL. 103 SEPTEMBER, 1931 No. 9

EDITORIAL

PHARMACEUTICAL DISCOVERIES

MUCH has been written concerning discoveries by chemists and physicians, but very little on the subject of discoveries by pharmacists. A review of the progress of science reveals that the pharmacist has been responsible for many famous discoveries which have added much to the welfare of humanity.

One of the greatest of all discoveries was that of morphine, the active medicinal principle of the opium poppy plant of the Orient. Morphine is held by many to be the greatest drug gift to mankind. Without this valuable drug to alleviate pain and to produce sleep the practice of medicine would be set back many years.

Morphine was discovered by an apothecary, Wilhelm Serturner, in his shop at Eimbeck, in 1815. It was named morphine after the God of Sleep, Morpheus. This discovery paved the way for the discovery of many other active constituents, such as codeine, quinine, strychnine, and emetine, all essential medicines.

Codeine, one of the other constituents of the juice of the poppy plant, was discovered by a pharmacist, Robiquet. It is related chemically to morphine, but its action is much milder and it is widely employed by the physician to alleviate irritation and produce rest.

A French pharmacist, Bernard Courtois, while experimenting on seaweeds, noticed that a purplish-colored fume arose from the mixture. Through this accidental discovery, mankind was presented with that great gift, iodine, which today is one of the most important antiseptics and which is used for a number of complex and obscure ailments that defy other forms of treatment. During recent years a number of new antiseptics have been developed, but iodine still continues to command a place of first rank as an antiseptic.

We all know hydrogen peroxide, sometimes referred to simply as peroxide. This medicinal preparation and invaluable industrial bleach was the result of scientific investigation in 1818 by Thenard, another French pharmacist.

Atropine, the active substance from belladonna, or the deadly nightshade plant, was discovered by the pharmacist Brandes. Atropine is an important drug, possessing a wide range of use. It dilates temporarily the pupil of the eye so as to enable the eye specialist to make a proper examination when required.

Another outstanding pharmacist was Scheele. He discovered oxygen in 1775, working independently of two other famous scientists, Priestley and Lavosier. Scheele likewise discovered chlorine, phosphoric acid from bones, tartaric acid from the substance known as argol or crude cream of tartar as found in wine casks. He is also credited with the discovery of hydrofluoric acid, a chemical reagent so powerful that it must be kept in specially prepared wax bottles, for it readily attacks glass. Because of this power, it is widely used in the etching of glass, the glass being covered with a wax film, leaving exposed only that part of the glass to be etched.

Antonie J. Balard, a pharmacist, first prepared bromine from salt as gathered from a salt marsh.

From the East Indies comes a very interesting drug, nux vomica. From this important drug, Pelletier, a pharmacist, working in conjunction with Caventou, extracted that powerful medicinal substance known as strychnine, widely used in medical practice for its stimulating effects.

Potassium acetate, an important medicine little known to the general public, but widely prescribed by physicians, was first prepared by the pharmacist Mueller, in 1610.

Seidlitz powders are one of the many important items sold in drug stores. One of the principal ingredients of seidlitz powders is Rochelle salt, named after the town of Rochelle, France. Rochelle salt was discovered by Peter Seignette, a pharmacist, in 1672.

It was a pharmacist, Guillaume Francois Rouelle (1672-1731) who classified chemical compounds into acid, basic and neutral, and who thereby paved the way for modern methods of measurement of degrees of acidity or alkalinity in place of the old litmus paper method.

One of the most important of all procedures in pharmaceutical practice is the one known as percolation, by means of which the pharmacist prepares what are known as tinctures and fluid extracts.

This important procedure was developed by Boullay, a pharmacist. Boullay is also credited with the discovery of picrotoxin, the active constituent of fish berries, a drug employed in combating body parasites.

Aromatic spirit of ammonia, prescribed by many physicians and kept in most home medicine cabinets, was developed through the work of a pharmacist, Jacob Sylvius.

An important milestone in the history of chemistry is the work of Wöhler, who showed in 1828 for the first time that organic materials could be made from inorganic substances, which finding is a fundamental phase of the development of present-day chemistry. There is evidence to indicate that an English pharmacist, Henry Hennel, preceded Wöhler by two years in a discovery of this kind by producing ethyl alcohol from inorganic materials or intermediate substances.

The study of colloids is one of the most important phases of modern chemistry. The foundation for this great industrial development has been in a large measure based on the discoveries of a Cincinnati pharmacist, John Uri Lloyd, who first, from his study of drugs, enunciated the fundamental principles of colloidal chemistry.

The use of accessory substances such as barium sulphate and bismuth salts in X-ray practice so as to render ray-transparent tissues such as the stomach readable on the film is said to have originated with Martin Wilbert, then apothecary to the German Hospital, Philadelphia.

The work of the pharmacist as a scientific investigator is still being carried on, as evidenced by the research being conducted in the laboratories of our many colleges of pharmacy, in some of our drug stores, and in drug manufacturing research laboratories.

And so the pharmacist has played and is playing an indispensable part in the progress of science. From out of those early apothecary shops, whose atmosphere was permeated with the odor of herbs and chemicals, there have come countless valuable discoveries in the fields of botany, chemistry, pharmacy, and medicine.

Today the pharmacist is equipped with modern apparatus in the laboratories of large manufacturing houses. In order to conduct modern research he must be a well-trained man, a graduate of a reputable college of pharmacy, and in many cases of post-graduate courses in chemistry, botany, and allied branches.

ORIGINAL ARTICLES

THE DRUGGIST HIMSELF

USUALLY the most ill-cared-for personage within the four walls of the drug store is the druggist himself, who is doomed for a certain time to rush up and down, before and behind his counters, serving irascible patrons, ironing out complaints, arguing about cut prices, warding off high-pressure salesmen, and trying to do a dozen tasks at once.

He may take a hurried lunch, or he may go without one. At the end of the day he crawls home exhausted in mind and in body, to dream of a depleted bank account or a call from the sheriff.

Too often, like Shakespeare's apothecary, the modern druggist, inwardly and outwardly, is "worn to the bone."

Health means much more than freedom from disease. Health has been defined as "that condition of the body that makes possible the highest enjoyment of life, the greatest constructive work, and that which shows itself in the best service to the world."

"One is only fit to serve, even as one is only fit to work, as one keeps oneself prepared to live most and serve best."

In the drug store one can purchase many things which will aid in promoting and sustaining health, but the druggist fails to follow his own prescriptions.

The druggist should be a living example of good health and right living.

The sources of good health and well-being are neither magical nor mysterious. They cost something, but they cannot be attained through money. The goal cannot be reached over night, nor in a week spent at a health resort. Vitality, strength and personal efficiency can be attained however through living within the stream of life.

A glance at some of the fundamental sources of good health may indicate wherein the druggist fails in its achievement.

Fresh Air—The "stale, musty odor" of the old-time drug store has in large measure disappeared, but too often the atmosphere is fetid and depressing. Our drug stores are often overheated and poorly ventilated. Some stores vainly try to neutralize this through the use of incense and perfumes. Open windows, doors and transoms, while helpful, do not give adequate relief. Polluted and

tainted air takes its toll upon the druggist, his clerks and patrons. Perhaps the modern systems of ventilation and air-conditioning might bring good results to the drug store.

The practice of living in the building where the drug store is located is not conducive to well-being. For a number of hours each day the druggist needs to separate himself from his store. For many hours during the day the druggist overstresses certain forms of energy and understresses others. Living within walking distance of the shop will help to restore the balance.

We can often walk away disease, and walk into health. Walking, and breathing in fresh air, with the chest expanded and the hips and arms in motion, calls into full play many organs of the body. This surpasses even an hour spent in a gymnasium.

Golf, tennis, running, stretching in due moderation may be helpful, but require caution.

We have come to know that the food which a man takes into his stomach is more important than the clothes which cover his back, or the money which goes into his pocket.

Marvelous progress has been made in our study of foods. Some of us may have gone a bit wild over vitamins, but there is a promise that we will eventually produce a better race of men and women. We have come to know that to fulfill its mission food must be of a proper kind, taken into the system at proper times and in proper amounts. We must eat according to a prescription. Tissue-building foods, energy-producing foods, and regulating substances in foods must be taken in by weight and measure.

The preparation of food has become a pharmaceutical problem. The druggist must assume the role of dietitian for himself and incidentally for his patrons.

The druggist is certainly one of the beings who needs proper rest and sleep. He requires eight to nine hours of sleep with, where possible, a short period of rest and relaxation (lying down) during the day. His hours of sleep should be in a cool room with opened windows. A walk or light exercise before retiring would be helpful.

Evening meals should be light, with avoidance of overeating and the possible foregoing of tea, coffee or "nightcap" cocktails. A warm (not hot) bath in the evening is sometimes helpful. More needed than all is a mind free from worry—a brain at rest.

The druggist should be a living example of cleanliness. He may well be a consumer of his own soaps, creams, lotions, powders, sham-

poos, tooth paste and eyewashes. All important is it that he give attention to his excretory organs.

Above all things, the druggist should beware of drugs. Drugs are to be administered only under the advice of a physician. Certainly a druggist should keep clear from dope, alcohol and the tar barrel.

Good physical health favors a good mental state. The man behind the drug counter needs to "think straight."

Efficiency is lowered, happiness decreased, through worry, fears, prejudices, pessimism; too great optimism and other emotions cause kinks in the brain cells that shape and fashion our daily lives. Intelligence, not feeling or emotion, should guide our actions.

From poor mental control there follows sensitiveness to criticism, brooding over minor ills, undue concern over one's own welfare, lack of interest in the welfare of others, a narrower view and hold on life.

The druggist must develop wholesome mental habits—that temper which Salesby characterizes as "half philosophic, half religious, half intellectual, half emotional, half rational acceptance, half faith."

In these days surveys are a popular and often a useful procedure. The druggist may well make a survey of himself, his surroundings and his relation to those with whom he comes in contact. In such a survey he will probably find things that are out of gear, things that have been allowed to fall into disrepair; he may even find rotten spots. He must examine one by one the foundation stones upon which success is to be built.

For the druggist, more perhaps than for many of his fellows, there must be maintained "a sound mind in a sound body."

The *druggist's place in life* is to *dispense—sell,* if you please—*health, well-being* and *comfort* to his *patrons* and to the *community.* He cannot do this unless he in his whole self attains the highest standard of efficiency.

FRED. B. KILMER.

A STUDY OF RHUBARB AND A QUANTITATIVE DETERMINATION OF SOME OF ITS CONSTITUENTS

By Peter Valaer*

THE principal source of rhubarb (Rheum Officinale Baillon) and other species of Rheum is in China and Thibet where it is grown. It consists of the dried rhizome and roots deprived of most of its cortex.

The official article is at the present time collected entirely in China and Thibet under the trade name of Chinese Rhubarb and is the only one recognized by the United States or England as standard.

The principal preparation of rhubarb is the fluid extract from 1000 grams of moderately coarse powder by U. S. P. Type A process using four volumes of alcohol and one volume of water as the menstruum.

Fluid Extract of Rhubarb differs from the fluid extract of cascara in that alcohol is used in its manufacture for extraction purposes instead of water as in the case of cascara. In many ways they seem to be similar, the principal difference being that rhubarb is more likely to throw down a residue when diluted with water. The Borntrager reaction is much more pronounced in rhubarb than in cascara. Instead of the yellow ether extract being in the ratio of 2 to 1 against the alkaline red solution, in the case of rhubarb it is in the ratio of 1 to 1. In other words, the yellow color in 1/16-inch cell is matched by a red of about the same strength in 1/8-inch cell. This will become clear to those who are not familiar with the method when they use the same.

Rhubarb is exclusively a Chinese product but strange to say, the Chinese rarely use it in liquid preparations and in the examination of many Chinese tonics and medicines of various kinds rhubarb is rarely found. It seems that Europeans and other Occidental nations appreciate its value more than the Chinese. When it has become necessary for Chinese to medicate their preparations in the United States through the requirements of our laws, cascara has been selected instead of rhubarb and even this American product has been shipped

*Chemist, Bureau of Industrial Alcohol, Treasury Department, Washington, D. C.

to China when the same kind of drug; to wit, rhubarb, is present in China in abundance.

The Italians physicians and manufacturers of medicinal preparations seem to appreciate rhubarb more than those of any other nation. Usually their rhubarb is treated with some sort of an alkali which interferes seriously with the color reactions, particularly the Borntrager reaction. This treatment is also detrimental to its physiological properties.

Formulas for the various rhubarb preparations listed in Pharmacopee Francaise (Codex Medicamentaris) do not call for the addition of any alkali.

The reduction of the efficiency of rhubarb due to the addition of potassium carbonate and other alkalies, is somewhat suggestive of the way whereby the efficiency of cascara in the manufacture of aromatic fluid extract of cascara is reduced to about one-half due to magnesium oxide used in the process outlined in U. S. P. No. 9 and how it is it is still further reduced by the addition of both magnesium and calcium oxide in the process outlined for the preparation of aromatic fluid extract of cascara in U. S. P. No. 10.

The most satisfactory method used in the Laboratory of the Bureau of Industrial Alcohol for estimating the quantity of rhubarb present in fluid extracts and other rhubarb preparations including medicinal preparations, containing more or less rhubarb is based on the Borntrager reaction (Z. Anal. Chem. 19 (1880) 165). When the group of drugs consisting of rhubarb, cascara, frangula, senna, and aloes, whose virtues depend principally upon the resinous hydroxyanthraquinone bodies and other anthraquinone compounds in solution are made acid and are extracted with ether and the ether extract made strongly alkaline with ammonia, a red color of a certain shade is caused to develop. Application is made of this test as a basis for quantitative estimation of, for instance, rhubarb in medicinal preparations under examination. Under certain carefully observed conditions the depth of color extracted by the ether and the color developed on the treatment with ammonia varies almost directly in proportion to the amount of rhubarb or other emodin-bearing drugs present. These readings are to estimate the free emodin bodies, after this a separate portion of the preparation is hydrolysed with concentrated sulphuric acid and the same process repeated. These readings are termed total emodin readings consisting of the color due to free and combined anthraquinone bodies.

The Lovibond's tintometer is depended upon to standardize the colors developed for these comparisons. A brief description of the apparatus is as follows:

The Lovibond tintometer used in these experiments is sold by Eimer and Amend, and is an instrument by which the depth of color of liquids can be accurately measured in degrees, placed in their position in a permanent color scale and registered for reproduction at any time. It consists of a graded series of standards made of colored glasses, numbered according to their depth of color and an instrument for holding the glasses, and the object to be measured.

The yellow ether extract is poured into the 1/16-inch cell and the color matched against the yellow slides. Ten cc. of the above extract is introduced into a 100 cc. Nessler tube and 10 cc. of strong ammonia (sp. gr. 0.90) added. The mixture is shaken, stoppered, and allowed to stand two or three hours. It is then diluted to 50 cc. volume and mixed. As soon as the ether portion rises to the top it is poured off and some of the red liquid poured into the ⅛-inch cell of the tintometer and carefully matched against the red tinted slides as in the manner before described.

The yellow extract and the emodin red produced vary almost directly with amount of rhubarb present and bear a simple ratio to each other. If the yellow ether extract reads 5 in 1/16-inch cell, the red developed reads about 5.0 in ⅛-inch cell.

This laboratory has made the examination of samples of preparations which were made with U. S. P. fluid extracts purchased from leading drug houses in the United States or prepared in this laboratory, each preparation was made to contain 15 minims of the U. S. P. fluid extract of rhubarb per fluid ounce in approximately 45 per cent. alcohol. The alcohol, solids and ash was determined by A. O. A. C. methods and the color readings were made by the following methods. The table below shows the results.

Method for color reading—Before Hydrolysis (free emodin): Extract 25 cc. of the preparation, made acid with 2 cc. N/10 H_2SO_4, extract 5 minutes with 50 cc. of ordinary sulphuric ether in separatory funnel, draw off aqueous liquor several times as it settles and take 10 cc. of the yellow ether extract and 10 cc. of strong ammonia and place in a colorimetric tube (Nessler) mix, allow to stand about two hours. The remainder of the yellow ether extract is read in 1/16-inch cell, then make the mixture in the Nessler Tube up to 50

cc. volume with water. Flick off the ether which rises to the top and read the red color in a 1/8-inch cell.

Method for color reading—After Hydrolysis (total emodin): Each preparation contained in each fluid ounce 15 minims of fluid extract. 25 cc. of each preparation was treated in an Erlenmeyer Flask with 2 cc. of concentrated sulphuric acid, shaken thoroughly and allowed to stand over night; refluxed over a steam bath for 30 minutes using a tube condenser. Transfer the material into a separatory funnel. Shake with 50 cc. of ordinary ether for exactly 5 minutes, allow to settle, draw off aqueous layer, shake and again allow to settle. Again draw off the remaining aqueous material. Repeat

No.	Color readings before hydrolysis Yellow 1/16" cell	Red 1/8" cell	Color readings after hydrolysis Yellow 1/16" cell	Red 1/8" cell	All the preparations in this table contain 15 minims F. E. rhubarb per fl. oz. Alcohol	Solids	Ash
10	6.4	5.5 red .5 yellow	11.7	9.1 red .5 yellow	45.12	1.02	.033
11	5.4	5.4 red .8 yellow	10.4	8.5 red .6 yellow	46.28	.89	.020
12	4.3	5.0 red 1.0 yellow	9.0	6.8 red .5 yellow	46.28	.62	.027
13	7.6	7.5 red 1.1 yellow	11.7	9.7 red .4 yellow	45.08	1.14	.062
14	3.4	4.5 red .5 yellow	10.7	9.5 red 1.0 yellow	45.12	.76	.025
15	8.0	6.7 red .7 yellow	13.0	10.9 red .4 yellow	45.52	.94	.030
16	3.4	5.0 red 1.2 yellow	10.4	9.9 red 1.0 yellow	47.96	.79	.021
17	3.3	5.4 red .6 yellow	13.1	11.1 red 1.7 yellow	48.04	.81	.010
18	4.7	4.2 red .5 yellow	7.6	5.9 red .4 yellow	47.60	.87	.035
19	3.2	5.1 red .5 yellow	11.5	10.5 red 1.3 yellow	47.60	.81	.015
20	4.8	5.3 red 1.0 yellow	13.7	11.0 red 1.0 yellow	47.16	.96	.025
25	3.7	3.0 red 1.8 yellow	14.5	10.7 red 2.5 yellow	47.04	1.22	.030
26	6.2	5.1 red 2.0 yellow	9.8	7.7 red 1.1 yellow	46.92	.91	.030
27	7.6	5.8 red 1.5 yellow	13.5	8.9 red .9 yellow	46.56	1.05	.035
28	10 0	8.8 red 1.0 yellow	15.9	13.8 red .8 yellow	46.48	1.15	.040
29	4.0	5.5 red .8 yellow	15.0	11.7 red 2.1 yellow	46.72	1.29	.025

Samples #28 and 29 were made from fluid extracts manufactured in laboratory—Samples 21 to 24 inclusive are not included in this table, being the same as 13, 14, 16 and 18, except 25% alcohol was used in their preparation instead of 45% alcohol which was used in all samples listed above.

this process until all the aqueous liquor is stripped out as completely as possible.

Take 10 cc. of the yellow ether extract and 10 cc. of strong ammonia and place in a colorimetric tube (Nessler) mix, allow to stand two hours, some of the remainder of the yellow color is read in 1/16-inch cell, then make the mixture in the Nessler tube up to 50 cc. volume with water, allow to settle, pour off the ether which rises to the top and read the red color in 1/8-inch cell.

It was an important matter to determine the alcohol actually necessary to keep Fluid Extract of Rhubarb in solution and to prevent its deterioration while in solution.

It was found that when preparations were made to contain the average dose of fluid extract of rhubarb, 15 minims per fluid ounce, using 25 per cent. alcohol as a menstruum, that there was more or less precipitation depending on the fluid extract of rhubarb used. With some manufacturers it was rather heavy—in some instances light, but there was a precipitation in each instance and the color readings used as a method of analysis showed this difference. The examination of the precipitate showed that it was rich in emodin material.

The table below will show exactly the readings and just how much deterioration happens in each case. Standard fluid extract of rhubarb made by four reliable manufacturing concerns was used in this experiment.

It would seem that either the manufacturer of tonics using fluid extract of rhubarb as an ingredient must be allowed alcohol around 45 per cent. in their product or allowance must be made for the prod-

	Free Emodin		Combined	
Number	Yellow 1/16″ cell	Red 1/8″ cell	Yellow 1/16″ cell	Red 1/8″ cell
13(45% Alc)	7.6	7.5 red 1.1 yellow	11.7	9.7 red 1.4 yellow
21(25% Alc)	4.4	4.4 red .9 yellow	7.6	5.9 red .8 yellow
14(45% Alc)	3.4	4.5 red 1.5 yellow	10.7	9.5 red 1.0 yellow
22(25% Alc)	2.6	3.12 red .9 yellow	9.0	9.5 red 1.4 yellow
16(45% Alc)	3.4	5.0 red 1.2 yellow	10.4	9.9 red 1.0 yellow
23(25% Alc)	2.6	3.3 red 1.4 yellow	8.0	7.7 red 1.3 yellow
18(45% Alc)	4.7	4.2 red .5 yellow	7.6	5.9 red .4 yellow
24(25% Alc)	2.6	2.5 red .5 yellow	4.2	3.6 red .6 yellow

uct when the alcoholic content is low when the preparations are examined by chemical analysis.

Thirteen and 21, 14 and 22, 16 and 23, 18 and 24 are made from the same fluid extracts, for instance 13 and 21 is the same except in making the preparations to contain 15 minims per fluid ounce, No. 13 was made to contain approximately 45 per cent. alcohol and No. 21 was made to contain 25 per cent. alcohol. The same is true of the three other combinations. Four fluid extracts of rhubarb from four large manufacturing concerns were used in this experiment.

While the above method is considered more satisfactory for the estimation for rhubarb in preparations, determinations were made on all the preparations listed above which contain in each fluid ounce 15 minims of fluid extract of rhubarb, by a method which is outlined below and which was once suggested by Dr. H. C. Fuller as an A. O. A. C. method.

Introduce 5 grams of the powdered drug or 5 cc. of the fluid extract or 25 cc. of a tonic containing as medication fluid extract of rhubarb into an Erlenmeyer flask of 500 cc. capacity; add 200 cc. of chloroform and 50 cc. of 25 per cent. sulphuric acid (70 cc. of sulphuric acid in water qs. 500 cc.); attach to a reflex condenser (water cooled) using cork stopper covered with tin foil. Apply low heat of Bunsen flame and allow the chloroform to boil for two and one-half hours. At the end of that time allow to cool and then transfer to separatory funnel, washing out flask with a little fresh chloroform.

Draw off the chloroform into another separatory funnel. Add 50 cc. chloroform to the acid mixture, agitate and after separation has taken place, run chloroform into that previously collected. Repeat the procedure three times for bark and fluid extract and twice for preparations. Discard the acid mixture.

Collect the chloroform shake-outs in an Erlenmeyer or distilling flask, recover about two-thirds of the solvent by distillation and pour the balance into a separatory funnel, washing thoroughly to remove final traces of anthraquinones; (use foil on all stoppers when recovering chloroform during distillation) agitate the chloroform with 25 cc. of 10 per cent. sodium hydroxide; draw off chloroform and subject to another treatment with 10 per cent. sodium hydroxide. Repeat again; draw off chloroform and wash with 25 cc. of water three times. (Two washings are sufficient with preparations containing one or two doses of cascara).

Unite the alkaline solutions and washings, add the excess of hydrochloride acid (15 cc. of concentrate HCl is usually sufficient) and shake out five times with chloroform. (Three times are sufficient with tonic preparations.) Discard the acid and wash the chloroform solution by shaking with 50 cc. of water; repeat, washing with 50 cc. of water; let settle completely, filter chloroform through cotton in stem of funnel into a distilling flask or Erlenmeyer flask and recover a portion of the solvent. Then pour the balance into a weighed dish, washing out distilling flask with chloroform; evaporate the solvent and dry at not over 100 degrees centigrade for 30 minutes, cool in desiccator and weigh. The weight represents the total anthraquinone bodies in the drug. Preserve the residue for the method described below. (If the residue should show any visible trace of white crystalline material wash again with water.)

Colorimetric Determination

Treat the residue of anthraquinone derivative obtained by the gravimetric assay described above with 10 cc. of 10 per cent. potassium hydroxide, wash into a 100 cc. graduated flask with distilled water and make up to volume. Ten cc. of this solution is then diluted with water to 50 cc., a portion introduced into a 1/8-inch cell of a Lovibond tintometer and matched against the red slides. Note depth of color and report degrees observed.

Transfer 20 cc. of the alkaline liquid by means of pipette to a separatory funnel, add an excess of hydrochloric acid and extract with 25 and 15 cc. portions of ether. Introduce a portion of this ether solution into a 1/16-inch cell of a Lovibond tintometer; match against the yellow slides, note depth of color and report degrees observed.

Fluid extract rhubarb U. S. P. made into preparations containing 15 minims per fluid ounce—residue and color readings below obtained on 25 cc. of the preparations treated as outlined in the extraction method which at one time was proposed as an A. O. A. C. method. See details above.

It was thought by some that using 10 per cent. of sodium hydroxide or potassium hydroxide in the above method was possibly too strong and may destroy some of the emodin bearing material. Apparently there is no particular advantage in using weaker alkali. Results with using 1 per cent. sodium hydroxide and potassium hydroxide show there was no particular advantage in using the diluted

solution but the disadvantage was that it was difficult to extract the emodin bearing material with 1 per cent. solution, requiring several extra extractions which is disadvantageous in an ordinary long method.

No.	Residue (grams)	Emodin Readings Yellow 1/16" cell	Red 1/8" cell
10	.015	.6	.7 red .1 yellow
11	.013	.6	.6 red .1 yellow
12	.020	.5	.5 red
13	.021	1.3	1.6 red .3 yellow
14	.020	.8	1.0 red .3 yellow
15	.015	.5	.6 red .1 yellow
16	.017	.6	.8 red .1 yellow
17	.019	.8	.9 red .3 yellow
18	.011	.4	.3 red
19	.020	.7	1.0 red .3 yellow
20	.024	1.0	1.2 red .4 yellow
25	.020	1.2	1.2
26	.030	.8	.9
27	.032	.9	1.1
28	.020	1.4	1.3 red .5 yellow
29	.020	1.3	1.3 red .6 yellow

It is suggested, however, that when this method is started it must be made continuous and the alkali must not be allowed to remain in contact with the emodin material over night or any long period as it does show some deterioration when this happens.

Conclusions and Suggestions

1. The average color obtained was 5.4 yellow in 1/16-inch cell and 5.4 red in ⅛-inch cell before hydrolysis and 12 yellow in 1/16-inch cell and 10 red in ⅛-inch cell after hydrolysis. The ratio of yellow to red being 1 to 1 before hydrolysis and 6 to 5 after hydrolysis. The red readings all require the addition of low reading yellow slides with the red to get the exact shade.

2. This first described method has been in use in the laboratories of the Bureau of Industrial Alcohol for some time and has proven

its usefulness and it is recommended as a means of standardizing U. S. P. rhubarb preparations, and in the analysis of all preparations containing rhubarb.

3. The second method shown is one that was seriously considered at one time as an A. O. A. C. method. As shown here it has been improved by making the details more definite. Although it gives a gravimetric figure, as well as color readings it is not regarded by users as valuable as the first method described, the latter being more economical as to time and material.

Much credit should be given Mr. George Mallory and Mr. Loren Burritt for suggestions and help on analytical results.

Responsible persons may secure the names of the manufacturers of these products by addressing the author, Room 422, Treasury Building, Washington, D. C.

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MORE ABOUT SYRUP OF FERROUS IODIDE*

By H. V. Arny and A. Steinberg

Introduction

THE DATA given in this paper are found in full in the inaugural dissertation of the junior author, presented in partial fulfillment of the requirements set forth for winning the Doctor of Pharmacy degree of Columbia University. Dr. Steinberg's "Arbeit" covers 339 typewritten pages describing two years of research on the subject of the deterioration of chemicals under the influence of light. Details as to work on any one of the thirty-five chemicals and preparations studied constitute a paper in itself and so at this time our findings on Syrup of Ferrous Iodide will be the only topic discussed. At the Miami meeting of the American Pharmaceutical Association a highly condensed summary of the entire research will be presented.

Historical

The senior author is one of the many investigators who have studied the problem of the deterioration of syrup of ferrous iodide. The bibliography given at the end of this paper includes only a few of the many articles published on the subject. For a full bibliography see the paper by Braford and Langenhan (1) that appeared in the 1927 *Journal of the American Pharmaceutical Association* which contains a bibliography of eighty-eight items. These articles plus the work carried out by the senior author of this paper puzzled rather than informed him on several points, concerning deterioration of the syrup, but the present paper, we believe, satisfactorily explains these puzzling anomalies.

Apparently Maisch (2) was the first to point out the interesting fact that a sample of the syrup that had turned brown could be restored to its original color by exposure to sunlight. Horn (3) found that boiling the finished syrup accomplished the same object. Others have found that the addition of iron wire or reduced iron to a discolored sample is likely to restore its original green color.

The practice of adding chemical preservatives to the syrup began in 1860 when Mayer (4) recommended the use of hyposulphite of soda. In 1876, Judge (5) advised the use of hypophosphorus acid.

*Read at the fifty-third annual convention of the New York State Pharmaceutical Association, Richfield Springs, N. Y., June, 1931.

As to cause of discoloration of the syrup, Maisch (2) found that it was due to liberated iodine. On the other hand, Haussmann (6) claimed that the darkening was due to the caramelization of the sugar and this theory has been repeated by a number of investigators. The experiments of the senior author of this paper indicated that both theories as to the darkening of the solution were correct. Some samples of the syrup did respond to tests for free iodine while other samples did not. In the case of some samples, the green color of the syrup could be restored by exposure to sunshine; in the case of others, the syrup became actually darker on exposure to the sun. This was the puzzling situation that Dr. Steinberg's work has cleared up.

Experimental

The original object of Dr. Steinberg's experiments with Syrup of Ferrous Iodide was the study of the influence of light upon this pharmaceutical. Details as to effect of light, will be discussed at length in the proposed A. Ph. A. article, so these details may be reduced at this time to the statement that samples of the same U. S. P. syrup were stored in seven types of glass bottles (1 flint, 2 amber, 1 blue and 3 green), were exposed to (a) direct daylight (b) were kept in diffused light on a shelf in a closet with glass doors and (c) were kept in a dark closet in our "dark room." Five separate samples were exposed to daylight and were examined at the end of one month, two months, four months, six months and one year respectively. The results may be summarized as follows:

1. The syrup (which assayed 6.54 gm. per 100 cc. when fresh) showed only slight iodide loss in all types of exposure (lowest figure after one year 6.33 gm. per 100 cc.).

2. All samples of the U. S. P. syrup in incompletely filled bottles turned brown in all types of exposure and all after six months had a caramel odor. The caramelization increased as per time of exposure and the darkest were those exposed to sunshine.

All samples of the U. S. P. syrup in incompletely filled bottles exhibited after standing the sediment (or scum) noted by one of us in a previous investigation (7). None of the samples responded at any time to the test for free iodine. These experiments indicated that light was not the cause of deterioration.

Authorities cited above indicate that in the case of certain samples of Syrup of Ferrous Iodide exposure to direct sunlight actually restored the green color of a discolored syrup.

Our work in 1929 (7) indicated that the answer to the riddle was the presence or absence of hypophosphorous acid, so the present authors turned to the study of the syrup made *without hypophosphorous acid*. Two samples of this type of syrup were prepared; one 5 per cent.; the other 10 per cent. FeI_2. One-half of each batch was poured into small completely filled bottles; the other half into half-filled bottles. All of these bottles were stored in a dark room and examination of the half-filled bottles one week later showed a dark brown ring at the surface of the syrup, which was gradually working downward. In the same period of time the syrup in the completely filled bottles remained the original pale-green color. Four months later, the same conditions obtained; the syrup in the completely filled bottles being unchanged; that in the half-filled bottles being brown almost to the bottom of the container. Some of these brown samples of the syrup (containing no hypophosphorous acid) were then exposed to direct sunshine and another set were still kept in the dark as a control. Those exposed to the sun returned to their original attractive green tint within two hours, those in the dark retaining their brown color. This experiment was repeated with the same sample several times with the same result. Kept in the dark, the sample turned brown; exposed to sunshine, the green color was restored.

In our previous work (7) we noted the curious fact that our sample made without hypophosphorous acid after it had turned brown indicated the presence of free iodine by the starch paste test, but did not respond to the chloroform test. The present authors therefore repeated this experiment with the samples which they had used in those operations just described. Again they found that the brown samples when shaken with chloroform failed to transmit a pink color to the latter solvent; and again they found that their brown samples of 1930 turned starch-paste blue. As a matter of confirmation, a brown syrup was shaken with chloroform and when the latter solvent separated from the syrup, a thin starch solution was layered upon the top of the syrup. The result was a chloroform layer devoid of color, a syrup layer that was still brown and a starch solution layer that was dark blue. As a control, plain syrup made brown with Lugol's solution was shaken with chloroform; the iodine instantly passed from the syrup layer to the chloroform layer.

We also verified the Horn experiment by warming our brown syrup of ferrous iodide (without hypophosphorous acid) on a water-

bath. This gentle heat caused the return of the green color, not only once, but also on the same sample kept a month longer until the brown color had been produced again.

The effect of sealing was also tried out on our syrup made without hypophosphorous acid. One portion was sealed in an ampul; a second was placed in a small pyrex test tube and tightly stoppered with a cork; a third was placed in a pyrex test tube which was stoppered with a pledget of absorbent cotton. In sunlight all three samples of the syrup remained the original light green color. In darkness all three turned brown and showed presence of free iodine. In all of these cases, including those where the sealed ampul was employed the air present in the container was sufficient to oxidize the green syrup to a brown color.

Conclusions

1. The color of the glass container has apparently no effect in the preservation of Syrup of Ferrous Iodide.

2. Syrup of Ferrous Iodide U. S. P. (containing hypophosphorous acid) is for a time more stable than that prepared without hypophosphorous acid. However, when the strictly official syrup turns brown its green color can be restored only by addition of stabilizers.

3. Syrups of Ferrous Iodide made without hypophosphorous acid can be preserved perfectly in completely filled bottles. Samples in partly filled containers will turn brown rapidly when kept in the dark, but the green color is quickly restored by bringing into sunlight. On the other hand Syrup of Ferrous Iodide containing hypophosphorous acid becomes permanently darker when exposed to sunlight.

4. The darkening of the syrup made with hypophosphorous acid is due to the caramelization of the sugar and such samples fail to indicate the presence of free iodine. On the other hand, the darkening of the syrup made without hypophosphorous acid is due to the liberation of free iodine as shown by the starch paste test.

5. The darkened syrup made without hypophosphorous acid responds to the starch paste test for free iodine but not to the chloroform test for the same element. This suggests the possibility that the iodine may form some loose combination with sugar, not decomposed by chloroform, but changed by the other carbohydrate, starch.

6. In our opinion, the syrup made without hypophosphorous acid is a product superior to that containing the acid. The acid serves as a preservative during a few months of contact with the air but

when the sample turns brown there is no way (other than chemical) to restore its original color. On the other hand, the dark color of a syrup made without hypophosphorous acid can be restored to its original green by action of sunlight or by warming on a water-bath.

7. Syrup of Ferrous Iodide (without hypophosphorous acid) can be kept perfectly by storing in completely filled bottles of suitable dispensing size, kept preferably in direct sunlight. The darkening is due to oxidation and apparently the sun's rays prevent this oxidation. As one of us has already pointed out (7) invert sugar is a better stabilizer for this group than is sucrose.

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WHO IS TO DISPENSE THERAPEUTIC AGENTS INTENDED FOR HYPODERMIC AND INTRAVENOUS INJECTIONS?*

By Louis Gershenfeld, Ph. M., B. Sc., P. D.

Professor of Bacteriology and Hygiene, Philadelphia College of Pharmacy and Science

IN THE State of Pennsylvania, Senate Bill No. 611 has recently been enacted and is ready for the Governor's signature. Therein we find the clause: "Remedial agencies that are administered hypodermically, intramuscularly or intravenously, all medicinal substances containing barbituric acid or its compounds (and all medicinal substances containing coal tar derivatives), and biologicals (except those biologicals distributed to State and County Health officials) and medicines containing substances of glandular origin (except intestinal enzymes) shall be sold only by registered pharmacists or assistant pharmacists employed by or conducting a registered pharmacy." We also find the statement that "Nothing in this act of assembly shall be construed so as to prevent an authorized practitioner of medicine from administering or dispensing such drugs to bona fide patients as he or she shall deem necessary."

Concerning preparations intended for hypodermic use, what has been gained by this legislation? The only item in this class that I can think of which merchants other than pharmacists may offer to the laity for sale is insulin. Some physician supply houses may stock ampuls and biological products but the latter as well as those manufacturers who sell direct to the physician are probably not affected if they sell only to the medical profession or if necessary the employ of only one registered pharmacist in their establishment will avoid any complications in the future. One is therefore safe in saying that this law did not nor can any similar statute aid much in placing the pharmacist in the position to serve as the sole dispensing medium for such preparations.

It is a known fact that ampuls and biologicals are being used or are displacing in increasing quantities some of the drugs as therapeutic agents. The prescription department and the income of its owner suffers unless these products are handled by pharmacists. And what is just as important to note is the fact that the direct sale of

*Read before the Pennsylvania Pharmaceutical Association, June, 1931.

such preparations by manufacturers or distributors to the physician who dispenses them results in the extension of dispensing of other therapeutic agents by these members of the medical profession.

Students in pharmaceutical courses today receive valuable information concerning such products but instead of taking advantage of the opportunities to make profitable use of their scientific training they frequently decry the practical use of the latter.

In my judgment there is only one way for the pharmacist to become the sole dispenser of biologicals and preparations intended for hypodermic use. He must place himself in a position to serve as the distributor of these medicaments. If the practitioner finds it convenient or necessary to resort to an increased use of sterile solutions of therapeutic agents for hypodermic injection (as found in ampuls) and to frequently employ biological products, the pharmacist as the best qualified individual should place himself in a position to supply these preparations.

Let us take the case of ampuls containing sterile solutions of medicaments. With a knowledge of sterilization and bacteriology, any pharmacist can become qualified to prepare sterile solutions for injections, place them in suitable containers, or fill them in ampuls and complete the entire operation, getting the containers ready for dispensing. The retail pharmacist today frequently presents the argument that the sale of these preparations in ampuls does not warrant him to go to all the trouble to prepare the finished product when he can buy and resell them without the trouble which would be required by the former operation. Even when only a resale is made, definite information concerning the preparation of these products and general information concerning ampul medication should be known. I wonder how many pharmacists actually know the large volume of ampuls sold directly to the practitioner, which business they could obtain, if they would expend as much energy toward handling these sales as they do in selling articles in side lines other than drugs.

Then there are many injections containing medicaments which practitioners would like to use but cannot for they are special formulas and are not regular stock products. Not only would the pharmacist sell the practitioner and make a profit on the sales of the ampuls containing any medicament (special formula or otherwise), but he would gain his confidence, and his position as a professional and scientific worker would be elevated. The net result you can imagine.

I have advised pharmacists to detail the physicians in their ter-

ritory so as to request them to prescribe for the ampuls desired, even if they are not prepared to make their own product or a special brand is requested. These are then dispensed as any other prescription, the patient being advised to bring one along each time he visits the doctor's office or they are to be available when the practitioner calls at the home of the patient. By this procedure the physician who, in many instances, pays for the injection is relieved of this expense, the pharmacist is benefited, not only due to the profit but because of the contact which he makes, and the patients gain in the long run for they are more apt to continue treatment with a resulting beneficial effect if they have paid for a half dozen or more ampuls than if such were not the case. There are of course some physicians who commercialize in the sale of these ampuls containing sterile solutions of medicaments or even biological products, in that they purchase these preparations for their patients and charge the cost and at times a little more than the cost to the patient. Many of the practitioners in this group are those who would not be classed as dispensers of drugs, who, in fact, would be highly incensed if they were so classified. Yet frequently they have no other alternative than to order direct from the manufacturer, for the pharmacist in their vicinity is not prepared to serve them along these lines. In other cases, especially in the manufacture and sale of sterile solutions in ampuls, the fact remains that the pharmacist is allowing the making and sale of the latter slip out of his hands, when he really should be prepared to dispense these products as he is prepared to dispense other preparations which require scientific knowledge and skill.

Biologicals are playing a prominent role in the prevention and treatment of disease. Why shouldn't the pharmacist provide and dispense these preparations just as he handles and dispenses viosterol, glandular products, and similar preparations, many of which he seldom if ever has occasion to combine with other medicaments? Biological preparations are just as much pharmaceutical preparations as are the galenicals or other products manufactured or processed from raw material. There is nothing which can increase the or add a pharmaceutical halo to a drug store or introduce an atmosphere of professional pharmacy as the presence of a proper refrigerator containing biologicals. Keeping the few biologicals on hand stored at room temperature is unsatisfactory, and many of such preparations quickly lose their potency if kept under such conditions. The use of the soda foundation refrigerator has its many drawbacks. Bio-

logicals should be stocked in those pharmacies where the owners are cultivating the prescription trade and the physician. The argument is frequently presented that a large outlay of funds is needed if a complete line of all biologicals of various manufacturers are to be stored. This is of course true but I think that in most localities you will find a complete line of only one manufacturer will suffice and to this there need only be added few isolated products manufactured by another concern. Where, however, the demand is great, it may be profitable to carry a complete line of biological products of several manufacturers or by arrangements with other pharmacists in the community some co-operative scheme may be worked out. Manufacturers of biological products have various workable plans between themselves and the drug trade which will help in caring for such problems as the occasion arises. It is important to remember that two important factors are necessary to a successful and profitable merchandising of biologicals: First—the dispenser of biological products should know all about them. Second—the community and physicians should know that the pharmacist is in a position to furnish biologicals when wanted. The latter is accomplished by the pharmacist through personal solicitation and educational literature, displays, etc., which the manufacturers of these preparations are more than delighted to supply. The first and perhaps the most important, the desirable information concerning these preparations, will enable the pharmacist to assist the physician in the selection of the proper bacterial vaccine or antimicrobic serum that may be required. Bacteriology will supply this knowledge concerning their nature, method of manufacture and standardization, mode of administration, dosage, keeping qualities and method of preservation. The pharmacist will then realize that proper storage is essential to the retention of the potency of these preparations, so that he will store them in the refrigerator and not in some drawer or on the shelf.

It is unfortunate that some pharmacists have seen fit to cut prices on biological products. Members of the profession who are interested in price cutting in general should give this their immediate attention as the latter more so than other kinds of price cutting concern the prescription department and professional pharmacy. The dispenser of biological products who handles and stores properly a complete line of these preparations, details the physician and advertises such products has an investment and a service which is deserving of the net

profit made possible by the sale of these preparations at the retail price designated by the manufacturer.

The pharmacist who will care for them properly should be the distributor of all free serums and biologicals supplied by city or state health departments. I know there are some pharmacists in rural districts who act in such capacity, but I believe this association should go on record that a nominal service or handling charge should be paid by the health department for storing and dispensing these products just as a nominal fee is paid by health authorities in some localities for prescriptions dispensed to the poor. In larger communities where the police department and station houses provide and dispense these preparations, I would strongly advocate that the local pharmaceutical organizations take steps to see that pharmacists who are prepared to handle such products should store and dispense them for the health department at a nominal service charge. I have personally found diphtheria antitoxin lying in a drawer over a hot radiator in a police station and what is even more serious have known where the police department did not report a lack of supply of diphtheria antitoxin so that none was available when called for by the physician.

I do not hesitate to say if the pharmacist, as the distributor of medicinal and therapeutic agents, stands in the way of progress for any long period of time and refuses to handle these preparations (for there are pharmacists who do not stock many of these products), some one will. There will result direct sales of such preparations from manufacturer to physician. Pharmacists, in neglecting to handle biological products and placing themselves in a position to prepare and dispense sterile solutions of medicaments are doing considerable harm to professional pharmacy. In addition to the monetary loss resulting from not selling these commodities, there is an additional loss due to the fact that the pharmacist fails to recognize that the physician and the laity will patronize the store where a professional atmosphere prevails.

The answer to the question who is to dispense therapeutic agents intended for hypodermic and intravenous injection lies in the hands of the pharmacist. Co-operation by members of the profession along these lines will help to maintain the status of the drug store as the dispenser of all therapeutic agents and reduce to a minimum dispensing by the physician. Will he take advantage of his scientific training

and his aggressive and skillful merchandising ability for the benefit of professional pharmacy?

It is within the power and grasp of the modern active pharmacist to re-establish himself in the position of practicing pharmacy professionally and to serve the physician and the public even better than he could serve them in the past. Bacteriology, the sanitary sciences and closely related subjects are at his call to help him restore pharmacy to its proper position, to help him add to his knowledge and increase his resources, to develop pharmacy as a leader among the medical services, and to help the pharmacist regain and increase his professional standing in the community.

THE PHARMACIST'S SHOW GLOBES*

By Aaron Lichtin, Ph. G.

Secretary of the Galen Pharmaceutical Society.

HISTORY is one of the greatest heritages of the civilized races. A correct knowledge of one's national history and a proper retrospect of a country's ethical, cultural, economic, military, social and political problems is at the very foundation of true patriotism. Just as the horizon is widened and patriotism strengthened by a knowledge of national history so does the knowledge of the past problems, struggles, defeats and victories of a profession such as ours—pharmacy—enhance professional pride and facilitates further progress.

What a wonderful panorama is unfolded by our profession's past. For some forty centuries it has been slowly and steadily stepping forward in the march of progress. Early in its history pharmacy was closely allied with medicine; in fact the same individual practiced both arts. In the thirteenth century of the common era pharmacies as such where medicines were sold began to spread rapidly—so does LaWall tell us in his "Four Thousand Years of Pharmacy." Maimonides, the celebrated Jewish physician, in a letter written in September, 1199, says, "Then I attend to my patients, write prescriptions and directions for their various ailments." [1] It is to be presumed that these prescriptions had to be filled by someone qualified in the practice of pharmacy.

The appearance of the drug store required some sign or mark to distinguish it from other stores. The necessity of a token of distinction makes the pharmacist's show globes a subject of considerable importance in pharmaceutical history. To appreciate the need of a distinguishing designation you must picture a shopping street of that period and the state of education of the shoppers. The streets—most of them—were narrow and winding. No street lighting was available. At night you carried your own lantern illuminated by a candle or natural oil. The people who knew how to read and write were few in number. Consequently places of business were designated by some sort of a token rather than by a painted or printed sign. Thus we find the Inn of Adam and Eve, a hostelry in London, in 1750 which was distinguished by a sign of the two Biblical char-

*Presented to Pennsylvania Pharmaceutical Association, June, 1931.

acters; the Lion Pharmacy in Odense, Denmark, established in 1549 was designated by the sign of a lion. These marks served to help the shoppers recognize their goal.

Pharmacists as a class adopted as a sign the heads of Galen (second century A. D.) and Paracelsus (1439-1541) "It was certainly from a noble spirit of doing honour to a superior desert, that our forefathers used to hang out the heads of those who were particularly eminent in their profession. Hence we see Galen and Paracelsus exalted before the shops of chemists." [2] Another distinguishing mark for a pharmacy and one which may still be seen in some localities is the mortar and pestle. "One of the signs originally used exclusively by apothecaries was the mortar and pestle, their well-known implements for pounding drugs. Among the celebrities who sold medicines under this emblem was the noted John Moore, author of the celebrated worm powder, to whom Alexander Pope (1688-1744) addressed some stanzas beginning:

> 'How much, egregious Moore, are we deceived by shows and forms;
> Whate'er we think, whate'er we see all human kind are worms.'

His shop was in St. Lawrence, Poultney Lane. Every week the newspapers contained advertisements proving, by the most wonderful cures, the efficacy of his powders." [2]

A drug store sign exhibited at a signboard exposition held in London, in 1762 bore the picture of three gollipots. A gollipot was

Fig. 1—Show Vases. These were popular in late 80's and early 90's of 19th century.

a glazed earthenware jar covered with parchment paper which was tied around with a string and used for storing solid extracts, ointments, etc. Among the early American signboards for a drug store was a picture of a carboy. This sign hung at 73 Westminster Street, Providence, R. I., from 1843 to 1850 and later at 31 Westminster Street in the same city.[3]

The beginning of the use of show globes as a distinguishing mark for a pharmacy could not be definitely ascertained. The difficulty to find any information on these globes is best illustrated by a quotation from a letter from the Smithsonian Institution, dated April 14, 1931. "We recently had occasion to make quite an extensive search for historical references pertaining to show globes. The search failed to disclose any authentic information on the subject. In fact none of the older and best known medical and pharmaceutical histories which we reviewed contained any information concerning these globes."

However, there are several conjectures which have been noted in regard to the origin of these globes which are worth relating. One is told by W. W. Figgis in the *J. A. Ph. A.*, Vol. 8, No. 5, May, 1919.

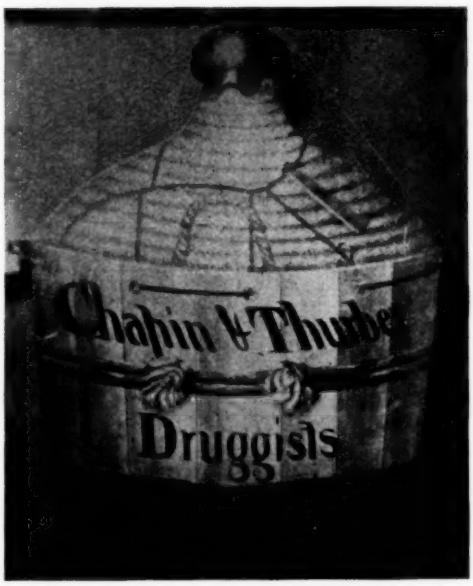
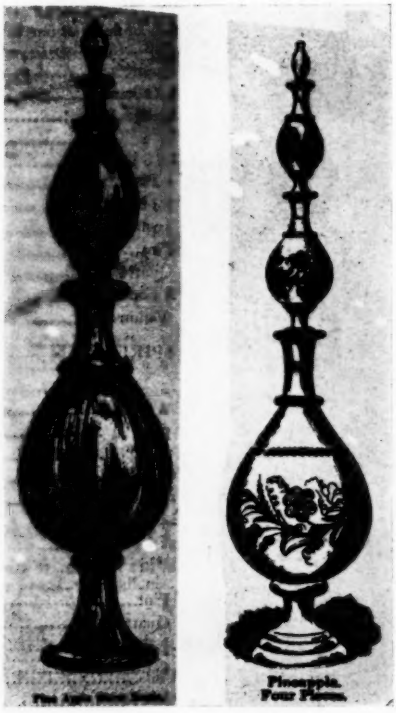


Fig. 2—Druggists' sign which hung at 73 Westminster Street. Providence, from 1843 to 1850 and later at 31 Westminster Street.

"When Julius Caesar invaded Ireland, a boat was sent ashore from the offing to locate the most advantageous landing place. A spot was selected on a shelving shore directly opposite a certain apothecary's shop, in the windows of which were certain large bottles containing drugs, which were in process of maceration, and the contents showed different colored liquids. On a promise of immunity as a reward, the arrangement was made that this apothecary would place lanterns behind these bottles to guide the landing of troops, which was made that night. The undertaking was successful, and to commemorate the same, an edict was issued by Julius Caesar that thereafter all apothecaries would be honored by being allowed to use colored carboys to identify their establishments."

Another conjecture is that the colored show bottles had their origin about the time of the great plague in London, in 1655, a time



(1) (2)

Fig. 3—"Pineapple" Style. (1) Made in 1874. (2) Made in early 80's of 19th century.

when people were compelled to reach the pharmacy without any loss of time. The colored light displayed served to guide the hurried messenger. No authentic information, however, was found to support these conjectures.

LaWall states the origin of the colored show bottles to be as follows. "Maceration had been employed for many centuries. Sometimes the directions for maceration required the operation to be conducted in the light for a certain number of days, and the large containers of tinctures in the process of manufacture, often two or three gallons in size, which usually stood in the pharmacist's front window evolved in later years into the show bottles of colored liquid which characterized the drug store of the latter part of the nineteenth century."

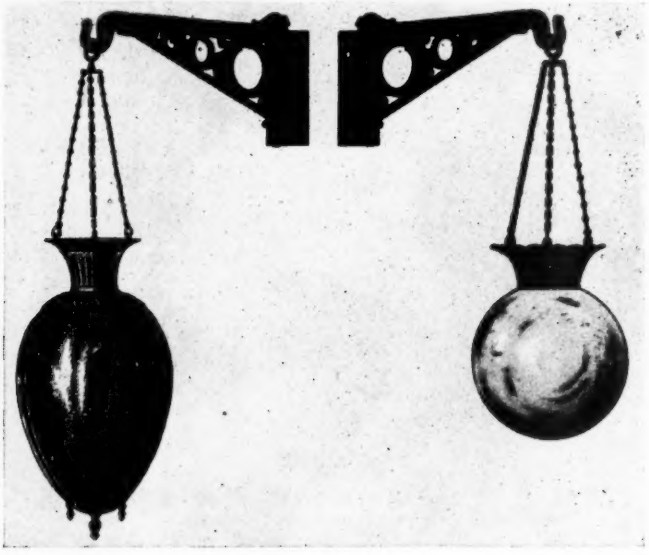
The sight of the show globes in a pharmacist's window are credited with inspiring a Scotch youngster, James MacKenzie to the study of medicine, who later became a celebrated cardiologist, and was knighted and appointed consulting physician to the King of Scotland. Sir James MacKenzie, as he is better known, born in 1853, was

Fig. 4—Three Graceful Show Globes, used in late 19th and early 20th century.

apprenticed as a youngster to a pharmacist with whom he remained till the age of twenty-one and then studied medicine in Edinburgh although he maintained an active interest in pharmacy throughout his life. He died in 1925. Judging from his biography the druggist's show globes were in use about the middle of the nineteenth century.[4]

The show globes are considered by the Pennsylvania Pharmacy Law as well as by the pharmacy law of other states as the recognized symbol of a pharmacy and regards the use of them by any other place of business as a violation. To quote from an official communication, "Section 15, Act 163, reads as follows—that it shall be unlawful for any person, firm or corporation to use the title: 'pharmacist,' 'assistant pharmacist,' 'druggist' or 'apothecary' except as authorized under this act . . . or in any manner by advertisement, circular, poster, sign, symbol, insignia . . . refer to the place of business as a drug store, pharmacy, etc. unless the place of business is a drug store or pharmacy duly licensed by the Board of Pharmacy.

"The Board believes that it is rather well established that the show globes are an insignia of a pharmacy and regards the use of them by any other place of business as a violation of this section of the pharmacy law."



(1) (2)

Fig. 5—Two Recent Types—(1) Made in 1920. (2) Made in 1930.

No matter how much one may delve into the origin and history of these beautiful colored objects, no real conception can be had of their appearance unless they are actually seen. A number of slides were prepared illustrating a number of various styles which have been used at various times. In collecting the material for these slides the writer was greatly helped by Mr. Joseph W. England, the Whitall Tatum Company and Mr. L. S. Williams, a retail druggist from Baltimore, who possesses the largest and most beautiful collection of these beautiful objects in glass in the country, fifty-one globes—to be exact.

The show globe is of the deepest significance to us, worshipers at the shrine of Aesculapius. It identifies us at once as practitioners of an ancient and honorable profession; it gives us a legal right to a symbol which may not be used by any other class of business, but a right which may be lost through lack of exercise. The show globe should be restored to its former dignity.

1545 South Seventh Street, Philadelphia.

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REPORT OF COMMITTEE ON DRUG MARKET
to the
PENNSYLVANIA PHARMACEUTICAL ASSOCIATION CONVENTION
at
Bedford Springs, Pa., June 16-18, 1931

IN THESE days of rapid development in industry and society when workers in every field are endeavoring to adjust themselves to and advance their particular industry, it is more and more evident that a closer scrutiny is being made of the quality of performance and product. In the pharmaceutical field quality has always been of prime consideration. Dealing as it does so intimately with human welfare, pharmacy, as a different kind of business, has its foundation in the fundamentals of quality and accuracy.

A review of the reports of this committee since its formation shows that the general standard of products has been high. This attainment has of course not been accomplished without effort, as constant supervision has been necessary by those who stress the ideals of quality and dependability. Considerable insistence has been required at times in order to impress and educate the careless and ignorant with the necessity of supplying or producing high-grade products. The return of substandard products by the purchaser and legal action by the various qualified governing bodies of our country have been very helpful in bringing about the proper condition. By no means are all of the substandard products of deliberate intent as an undetected mishap in manufacture or a subsequent change or deterioration of the product is oftentimes responsible.

Our report this year, considering the number of products examined, shows only a small proportion of inferior or substandard products. One of our contributors reports having found but six out of the five hundred samples examined that were not of standard quality. Some of them were only slightly subnormal. Approximately the same condition was found by other contributors as only a small proportion of the thousands of products examined under their direction were found to be of substandard quality.

The most interesting of our products are the crude drugs; they can be so easily contaminated with closely related drugs and even ignorantly substituted entirely for the authentic drug by unexperienced

persons. The condition under which they are grown also makes soil contaminations easy particularly in the case of roots and hairy leaves.

Among the substituted products we find a spurious berry offered for buckthorn berries; a root offered for marshmallow that was lacking in mucilaginous quality, and rhapontic rhubarb offered for the official variety. Occasionally drugs of doubtful authenticity are met such as aconite root, which we describe more fully later in the report. Drugs collected at the wrong time are also found, such as burdock root containing the second instead of the first-year root, lobelia collected when flowering, and blue malva flowers of poor color quality.

Drugs contaminated with soil, foreign seeds, stems, etc., are more common than other substandard ones. In this class we find Hungarian chamomile flowers and stramonium leaves containing excess foreign matter, psyllium seed with an excess of foreign seeds, pichi with an excess of stems, valerian with 20 per cent. of foreign roots, and wild yam containing stone root. One small lot of saffron contained an excess of moisture. Pipsissewa of N. F. quality was found to be practically unobtainable.

Many of the crude drugs were of exceptional quality such as belladonna leaves containing 0.53 per cent. of alkaloids, and red cinchona bark with two lots containing 9.7 per cent. and 9.33 per cent. of alkaloids, another lot however contained only 3.92 per cent. of alkaloids which is a good illustration of the wide range occurring in the active principle content of some drugs. A rather unusual occurrence was found in a lot of hyoscyamus which contained 0.138 per cent. of alkaloids; this drug is more likely to be close to the standard or oftentimes below it. Ipecac also has been of good quality, as only one lot has been below the U. S. P. standard. A particularly good lot of opium was received, which although in a rather moist condition, yielded 14.92 per cent. of anhydrous morphine. Substances such as asafetida and benzoin, which at one time were difficult to obtain in a sufficient degree of purity, were of good quality. Jalap and ipomea were also of very good quality.

Owing to the control in manufacture and the availability of suitable tests for the determination of purity, not much trouble is encountered with chemicals. A few instances of inferiority were met such as a lot of calcium lactate containing an excess of fatty acids, procain with an excess of heavy metals, and sodium chloride containing sodium citrate. One lot of caffeine was found to be anhydrous instead of containing one molecule of water as given in the U. S. P.

Other substances not included in the preceding groups and which were also inferior in some respects include balsam Peru not of U. S. P. quality, caramel having poor tinctorial quality and an acid, sour condition; dextrose containing dextrin, soft soap with an excess of water, kaolin containing carbonates, a lot of compound solution of cresol containing cresol not of U. S. P. grade, and a lot of powdered extract of hyoscyamus colored with methylene blue. Several lots of glass ampuls were found to have excessive alkalinity as high as 2.34 per cent. calculated as potassium hydroxide instead of not more than .014 per cent.

The following substances were examined in the laboratories of Sharp & Dohme, Robert McNeil, and Smith, Kline & French, during the period from June 1, 1930, to June 1, 1931:

ACID SULPHOSALICYLIC

Two samples had melting points of 108° C. and 110° C., respectively. The U. S. P. under reagents on page 484 gives "about 120° C." as the melting point.

H. H. SHULL.

ACONITE

Aconite is a drug that has caused a lot of worry; most supplies have the necessary activity, but whether they are Napellus is open to doubt owing to abnormal shapes and the number of roots that spring from the mother root, in some instances seven daughter-roots.

H. H. CROSBIE.

ASAFETIDA

Two lots of powdered asafetida contained 41.5% and 50.75% respectively of alcohol-soluble extractive. The U. S. P. standard is not less than 50% alcohol-soluble extractive.

H. T. HAEFELIN.

BALSAM PERU

A shipment was rejected some time ago because it did not conform to the U. S. P. requirements.

J. MERVIN ROSENBERGER.

BELLADONNA LEAVES

One sample assayed 0.53% of alkaloids. This is decidedly higher than the U. S. P. standard of not less than 0.3% of total alkaloids.

R. L. GREENWOOD.

BENZOIN

The alcohol-soluble extractive of two samples of benzoin was 83.5% and 79.5%. The U. S. P. standard requires not less than 75% alcohol-soluble extractive.

H. T. HAEFELIN.

BENZOIN, SUMATRA

A shipment was received that assayed below the U. S. P. requirements.

J. MERVIN ROSENBERGER.

BLUE MALVA FLOWERS

A lot was rejected due to the fact that the color of the flowers was not up to our standard.

J. MERVIN ROSENBERGER.

BUCKTHORN BERRIES

A spurious berry is again being offered for the genuine Rhamnus cathartica.

H. T. HAEFELIN.

CALCIUM CHLORIDE CRYSTALS C. P.

One sample assayed 59.07% anhydrous calcium chloride, whereas it should theoretically yield 50.66% anhydrous calcium chloride.

H. C. LUCKINGS.

CALCIUM LACTATE

Two lots were rejected because they did not comply with the volatile fatty acids test of the U. S. P.

H. C. LEIBHARI.

CAPSICUM

The non-volatile ether extractive content of two samples was 12.4% and 12.8%. The U. S. P. standard is not less than 12% of non-volatile ether-soluble extractive.

R. L. GREENWOOD.

CARAMEL

Several samples of poor quality caramel were offered during the year. They were generally weak in tinctorial power. One sample had a strong acid reaction and possessed a sour odor and taste.

H. T. HAEFELIN.

CAFFEINE

Commercial Caffeine is now being offered that is completely anhydrous. The U. S. P. gives caffeine as containing one molecule of water. Corresponding to not more than 9% of water.

R. I. GRANTHAM.

CHAMOMILE FLOWERS HUNGARIAN

An importation was refused delivery because of excessive foreign matter. This being a very difficult article to reclean, the goods were returned to the foreign jobber.

J. MERVIN ROSENBERGER.

CINCHONA

The alkaloidal content of three samples of Red Cinchona was 9.7%, 4.55% and 9.33%. One lot of Yellow Cinchona assayed 3.92%. The U. S. P. standard is not less than 5% of alkaloids of Cinchona.

KO SUTO.

DEXTROSE

One lot was rejected because dextrin was present and because sulphates were in excess of the U. S. P. allowance.

H. T. HAEFELIN.

GLASS AMPUL

Excess alkali was present in three lots of glass ampuls. They assayed 2.09%, 2.34% and 0.29% alkali as potassium hydroxide. Grade A glass should show not more than 0.014% potassium hydroxide.

H. C. LEIBHART.

GLYCERIN

One lot was rejected because 0.021% of residue remained after burning and 0.008% of residue after ignition. The U. S. P. allows not more than 0.015% of carbonaceous residue and not more than 0.007% of ignited or mineral residue.

J. J. FARLEY.

HYOSCYAMUS

One sample contained 0.138% of the alkaloids of Hyoscyamus. The U. S. P. requires the presence of not less than 0.065% of alkaloids.

R. H. BERESFORD.

IPECAC

The alkaloidal content of two lots was 2.06% and 2.14%. The U. S. P. standard is not less than 1.75% of ether-soluble alkaloids of Ipecac.

KO SUTO.

IPECAC

One sample of the ten examined assayed 1.44%, which is below the U. S. P. requirement of not less than 1.75% of ether-soluble alkaloids.

H. H. SHULL.

IPOMEA

The resin content of two samples was 18.6% and 15.9%. The U. S. P. standard is not less than 15% total resins of Ipomea.

H. C. LUCKINGS.

JALAP

One lot assayed 7.5% of resin. The U. S. P. standard is not less than 7% of resin of Jalap.

R. L. GREENWOOD.

KAOLIN

The examination of one sample of Kaolin gave a strong reaction for the presence of carbonates. The N. F. allows no carbonates.

H. C. LEIBHART.

LIQUOR CRESOLIS COMPOUND

One sample assayed 49.4% Cresol, but only 78.1% of the recovered Cresol distilled between 195° and 205° C. The U. S. P. requires that not less than 90% by volume of Cresol should distil between 195° and 205° C.

H. C. LUCKINGS.

LOBELIA

Lobelia is still offered containing mostly stem collected when fruiting. It has been difficult and costly to get the U. S. P. quality.

H. H. CROSBIE.

MARSHMALLOW

A substitute has been offered which is a sliced rhizoma with very little mucilaginousness.

H. H. CROSBIE.

MILK SUGAR

Two samples of the five examined did not comply with the U. S. P. test for a clear solution in boiling water.

H. H. SHULL.

MILK SUGAR IMPALPABLE

One lot was rejected because it was excessively dirty and would not be satisfactory for the manufacture of hypodermic tablets.

R. I. GRANTHAM.

MYDRIATIC LEAF DRUGS

The Mydriatic Leaf Drugs have been plentiful and of good strength, well above the U. S. P. minimum standard.

H. H. CROSBIE.

OIL PEPPERMINT

One lot was rejected because it had a distinct odor of spearmint oil contamination.

H. T. HAEFELIN.

OLIVE OIL

Two samples did not meet the U. S. P. chilling test, but passed all the other U. S. P. requirements.

R. I. GRANTHAM.

OPIUM

The assay of a five case lot imported from Jugoslavia showed 14.89% of anhydrous morphine. The shipment was received in a very moist condition.

KO SUTO.

PICHI

One lot was rejected because of the presence of an excessive amount of stems.

H. T. HAEFELIN.

PIPSISSEWA

Pipsissewa of N. F. quality has been practically unobtainable. Either the collectors do not know what 5% means or they do not realize that an official standard should be striven after. We have not recently come across any Spotted Wintergreen which was offered some while back as Pipsissewa.

H. H. CROSBIE.

POWDERED EXTRACT HYOSCYAMUS

One sample of the two examined contained methylene blue as an added color.

H. H. SHULL.

PROCAINE

Heavy metals were present in excess of the U. S. P. allowance in two samples offered as U. S. P. Procaine.

H. C. LEIBHART.

PSYLLIUM SEED

One shipment was rejected on account of not being properly recleaned. It contained an excessive amount of foreign seeds.

J. MERVIN ROSENBERGER.

RHATANY

Practically all the supplies offered have had a dark brown wood, whereas the U. S. P. specifies "yellowish or pinkish-white"; this may be a seasonal variation.

H. H. CROSBIE.

RHUBARB

There have been several lots of Rhapontic Rhubarbs offered and good U. S. P. quality has not been easy to get.

H. H. CROSBIE.

SAFFRON U. S. P.

A small lot was found to be of unsatisfactory quality due to an excess of moisture.

J. MERVIN ROSENBERGER.

SODIUM CHLORIDE

One sample of the seven examined was contaminated with sodium citrate.

H. H. SHULL.

SOFT SOAP

Two samples contained 57% and 54.75% of moisture. The U. S. P. allows not more than 52% of moisture.

J. J. FARLEY.

STRAMONIUM LEAVES

A shipment was received containing an excessive amount of foreign matter. This lot was recleaned and made to conform with the standard requirements.

J. MERVIN ROSENBERGER.

VALERIAN

Valerian has been found that contained about 20% of extraneous roots, a tasteless, odorless, woody, creeping rhizome.

H. H. CROSBIE.

WILD YAM

Wild Yam has been coming through mixed with Stone Root, and it has been necessary to hand pick most shipments.

H. H. CROSBIE.

The following table shows the results of the pharmacological assay of 20 samples of crude drugs made in the Pharmacological Laboratory of Sharp & Dohme, Inc., during the year of June 1, 1930, to June 1, 1931:

Drug	No. Samples	Assay		Standard	
		Lowest	Highest	Above	Below
Aconite	2	117	142	1	1
Apocynum Root	1	—	92	—	1
Cannabis	5	100	116	5	0
Digitalis	6	102	135	6	0
Ergot	1	—	115	1	0
Squill	4	93	105	3	1
Strophthanus	1	—	90	—	1
Total	20			16	4

DR. J. C. MUNCH, A. QUICI.

Respectfully submitted,

J. G. ROBERTS, Chairman,
J. W. E. HARRISSON,
J. MERVIN ROSENBERGER,
GEORGE A. SLOTHOWER.

MEDICAL AND PHARMACEUTICAL NOTES

EYE LOTION CAUSE OF SKIN ERUPTION—An unusual case of skin disturbance caused by an eye lotion containing procaine was reported by Dr. Bart M. James, of Newark, N. J., to the meeting of the American Medical Association.

The patient had been suffering with swelling and inflammation of her eyelids for six months. When all kinds of treatment had been tried unsuccessfully, she consulted a skin specialist. She had lost considerable weight, was in a nervous condition and unable to sleep.

The eye drops had not been considered at first, because the patient had been using them for several years, whereas the skin disturbance had only appeared within the last six months.

Skin tests were then made with the usual vaccines and pollens and in addition with all the cosmetics the patient had been using, including rouge, mascara, face powder, cold cream, lemon wash, hair tonic, the tortoise of her eyeglasses, and the eye drops.

All except the eye drops were negative. The spot where the eye drops had been tested showed an eruption like that on the eyelids on the second day after the test. It was found that the procaine contained in the drops gave the same result with the skin test.

When the eye drops were discontinued, ointment put on the eyes and a few X-ray treatments given, the skin disturbance cleared up.—(*Science Service.*)

SUBSTANCE OF DIGESTIVE JUICE PREPARED PURE—The digestive ferment of the stomach, that dissolves the starch in foodstuffs and makes it available for the energy needs of the body, has been prepared in the pure state for the first time in the chemical laboratories of Columbia University.

This marks an important step towards finding out what these complicated ferments really are, a problem that has hitherto remained unsolved because they could not be obtained pure.

Prof. H. C. Sherman, who is well known as an authority on the vitamins, and two associates, Prof. M. L. Caldwell and L. E. Booher, announce their accomplishment in a report to the journal, *Science*.

Starch under the action of this ferment is converted into malt, and this being also the first step in the preparation of fermented liquors from grain.

The crystals of diastase or amylase, as the starch ferment is called by chemists, were obtained from solutions of the pancreatic extract in a mixture of alcohol and water. The crystals show resemblances to proteins, those nitrogen-containing compounds which form so large a part of the stuff of the body. Because of this the crystallization must be carried out with very slight changes in temperature and the amount of acid in the solution controlled accurately.

This is the third digestive substance to be isolated. Protease, also found in digestive juice, which digests proteins like gelatin or the casein of milk, was recently crystallized by Dr. John H. Northrop and Dr. M. Kunitz at the Rockefeller Institute for Medical Research at Princeton, N. J.

Urease, the enzyme that transforms urea into ammonium carbonate for plant use, was first made crystalline in 1926 by Dr. James B. Sumner at the Cornell Medical College.

The enzymes or ferments play a very important part in the life processes of plants or animals. They accelerate chemical reactions without themselves being used up in the process. Chemists call such substances in general catalysts; though enzymes are very special kinds of catalysts which are extremely unstable and therefore difficult to handle in the laboratory.—(*Science Service.*)

Sodium Thiosulphate for Ringworm of Feet—A bath with a common chemical, sodium thiosulphate, effectively wiped out ringworm

of the feet in the Albany Junior High School where hundreds of the pupils representing at least half of the total enrollment had the disease, Dr. William L. Gould, of Albany, has reported to the American Medical Association.

Ringworm, also known as toe itch, toe scald, fungus foot, athletic foot, Hongkong foot or Shanghai foot, is very common, very old and very widespread. One-half of all adults have it at some time, according to the U. S. Public Health Service. Nine-tenths of people who habitually attend gymnasiums have it. It is an infection with a fungus. Healthy carriers of ringworm exist just as in other contagious diseases. These people have the disease without symptoms, but are a source of danger, as they may at any time acutely affect themselves or others. Peeling of the skin between the toes or around the nails, the formation of water-like blisters, cracking of the skin, itching and burning are found in various types of ringworm.

Statistics from colleges show that less than half as many girls are affected as boys. The reasons generally given for this are that girls' gymnasiums are better equipped and more sanitary, girls never go barefoot, have less occasion to perspire, keep better personal hygiene, and wear lighter, ventilated shoes which they change oftener.

The condition was discovered in routine examination of the pupils at the Albany school. Various measures, such as excluding the children from gymnasium classes and swimming pool, and swabbing with iodine and mercurochrome, were tried, without success. Then the sodium thiosulphate bath was installed between the locker and the shower rooms. Each pupil on the way from shower to locker room immersed his feet in the chemical bath. In the process the solution got well splashed over the locker room floor, so that from the time the pupil left the shower until the time of dressing, his feet were in constant contact with the chemical solution. Even a very weak solution of the thiosulphate was effective, so that by starting the bath with a rather strong solution of from 10 to 15 per cent. it did not become too dilute by the dripping of plain water into it from the pupils' feet that came wet from the shower.

VITAMINS A AND B PRINT INITIALS ON PHOTO PLATES—Two of the vitamins, A and B, apparently give off some kind of radiation that will affect the emulsion on a photographic plate in the same way that light and X-rays do. This is indicated by experiments performed by two women scientists, Sophie Botcharsky, of London, and Anna Foeringer, of Paris.

In the British scientific journal, *Nature,* they report as follows:

"Photographic plates were covered with aluminum foil and letters were cut out of the foil covering the glass side. Extracts of vitamins A and B, biologically tested, were used to paint the letters VA and VB on the glass side. The vitamin A used was ether extract of dried ox-liver, the solvent being removed in nitrogen. Vitamin B was water extract of purified brewers' yeast. The plates, wrapped in black paper, were left for three days; on development, clear images of the letters were obtained.

"To confirm the results, vitamins A and B were sealed in two separate glass tubes, and the experiment was repeated. Very sharp images were again obtained.

"An extract of vitamin A prepared in a Paris research laboratory was investigated in the same way. It also gave positive results.

"Vitamins destroyed but not carbonized did not affect the plates.

"Two solutions, one ten times stronger than the other, of vitamin A in paraffin oil and vitamin B in water, were compared. The plates showed clearly difference in strength. Control experiments of pure solvents gave unfogged plates.

"It is interesting to note that the effect of vitamin B is similar to that of vitamin A, although the two vitamins are of different origin.

"The experiments were repeated several times, and the same definite effect was present. We are proceeding with our research into these effects."

STAINS CAUSED BY DRUGS; METHODS FOR REMOVAL OF—I. G. Farbenindustrie.

Albargin—Recent stains of albargin are easily removed from linen fabric by means of soap and water. Old stains, which have been

darkened by exposure to light, must be soaked in hot 1:10 or 1:5 solutions of sodium thiosulphate until the marks disappear.

Peruvian Balsam—These are difficult to remove. Chloroform is often effective.

Chrysarobin—Benzene, chloroform or alcohol are the best solvents.

Aniline Dyes—Usually the best results are obtained by preliminary treatment with solution of chlorinated soda, or with hydrochloric acid, followed by thorough rinsing in water. Very resistant stains should first be soaked for several hours in a 1:1000 solution of potassium permanganate, then treated with water, or with a solution of oxalic acid.

Silver Nitrate—Stains on the skin may be washed off with a 1:10 solution of mercuric chloride; or with a similar solution of ammonium chloride. Silver marks on linen should be first treated with solution of potassium cyanide and a 1:10 solution of potassium iodide. The moist area is then treated with sodium thiosulphate solution to remove the traces of silver iodide left.

Protargol—Fresh stains may be removed with soap and water. Old stains should be treated as directed for silver nitrate; or better still, treated with a mixture of hydrogen peroxide and ammonia, or with solution of ammonium persulphate.

Rivanol—Linen or cotton fabrics must be soaked in a cold 1:10,000 solution of potassium permanganate containing 12.5 per cent. of acetic acid, in a capacious wooden tub or enamelled vessel so that fabric can be freely moved about in the liquid. After soaking for three or four hours with frequent stirring, rinse well in plenty of clean water. The material will be stained brown by the permanganate; the wet fabric is then immersed in a bath of 4 per cent. solution of sodium bisulphite or a dilution of 1 part of commercial bisulphite liquid with 9 parts of water. It is then transferred to an acid bath, which may be made with equal parts of 30 per cent. acetic acid and water. The material is finally thoroughly rinsed in plain water. Flannel, woollen, and flannelette fabrics cannot be treated as above. They should first

be soaked in hot water to which 12.5 per cent. of strong acetic acid (30 per cent.) has been added and left, with frequent stirring, for half an hour, then thoroughly rinsed in plain water. If necessary, the treatment must be repeated. If exposure to light has caused very dark stains which are not removed completely by the above treatment, the fabric must then be soaked in a bath of hot water to each litre of which 500 cc. of acetic acid (30 per cent.) and a tablespoonful of hydrogen peroxide (3 per cent.) have been added.

Trypaflavine—Linen or cotton fabric is first rinsed in the usual manner and wrung out, then boiled in a solution containing 2.5 per cent. of aflavol; finally rinsing in plain water. Woolen cloth should be treated if possible at once, while the stains are still damp; then washing with very hot water containing a little soap will be sufficient, followed by thorough rinsing. If the spots have dried, the stained area is first washed well with hot water. It is then treated, for fifteen minutes, with a dilute 2:1000 solution of hydrochloric acid at 50° C. Distilled or rain water should be used.—(*J. O. B., J. Pharm. Belg.*, 1930, 12, 663, *through Quar. Jour. Pharm. & Pharmacol.*)

Ergot Injured if Not Kept Cool—Ergot, that highly important drug when prepared into its fluid extract, must be kept cool or it will spoil, Drs. Maurice I. Smith and E. F. Stohlman, of the National Institute of Health, Washington, told members of the American Chemical Society at the recent meeting. They also found that oxidizing substances added to the extract hastened its deterioration, whereas reducting substances, which absorb oxygen instead of adding it, aided in its preservation.

Arsenic Poisoning Widespread, Beauty Parlor Clippings Show—Hair clippings collected from beauty parlors and barber shops and subjected to chemical analysis show that very many of us are carrying around mild cases of arsenic poisoning without ever suspect-

ing it. It may become serious enough to cause "patch baldness," or bleachings or discolorations of the skin.

This evidence that a considerable proportion of our population are "arsenic carriers" was presented by Drs. C. N. Myers and Binford Thorne, of the New York Skin and Cancer Hospital, before the American Chemical Society here. The arsenic comes from the widespread use of poison sprays to protect fruit and other crops, and even from clothing made from cotton sprayed to keep off boll weevil.

MODIFIED LABARRAQUE'S SOLUTION AND "ATHLETIC FOOT"—A common chemical used in purifying city water supplies, sodium hypochlorite, and the major ingredient in Labarraque's solution, has been found to be an effective preventive of ringworm infection of the feet by two Buffalo workers in medical research, Dr. Earl D. Osborne and Miss Blanche S. Hitchcock. This disease, also known as "athletic foot" and similar nicknames, has spread spectacularly with the postwar rise of sports involving the use of common dressing rooms and other gathering places where athletes trample around barefooted for a time. There the spores of the fungi that cause the disease are spread from foot to foot, later causing irritation, cracks and itching watery blisters.

Dr. Osborne and Miss Hitchcock state in their report to the official publication of the American Medical Society that they have not been able to find a record of sodium hypochlorite being used or suggested as a fungus-killer before. They made some preliminary trials with cultures of various fungi in test tubes, using solutions of the chemical in concentrations stepped up from one thousandth of one per cent. to one-half of one per cent. The latter concentration seemed the most effective, and was chosen as standard for a clinical trial.

With the co-operation of the physical training department of the Buffalo high schools, heavy rubber pans were installed in all the gymnasiums, and students going to and from gymnasium classes were required to wash their feet in a one-half per cent. solution of sodium

hypochlorite. The solution was renewed every day. In a new high school a shallow "well" for the solution was built into the corridor passing from the dressing room to the showers. Later, the strength of the solution was increased to a full one per cent. because of possible dilution through use.

The results of the experiment are reported as most encouraging. The spread of the infection was completely checked. "Our records fail to show a single new case, although numerous ones have appeared from the surrounding towns," the two experimenters report.

The hypochlorite solution, however, is not to be looked upon as a cure for already established cases. The report continues: "So far as cure of the disease is concerned, we do not believe that 0.5 per cent. solution hypochlorite or even 10 per cent. sodium hypochlorite would be any more efficacious in curing an established case than any other methods employed at present in the treatment of this stubborn condition."—(*Science Service.*)

STEVIOSIDE, THREE HUNDRED TIMES SWEETER THAN SUGAR—A natural substance three hundred times sweeter than cane sugar, rivaling some of the coal-tar products of chemical laboratories, has been shown by two French chemists to consist of a chemical union of common glucose and another compound which has little or no taste. United, they are intensely sweet; divided, they are not even as sweet as ordinary sugar.

The compound bears the chemical name "stevioside," because it occurs in a South American plant known to botanists as Stevia. The plant itself was first introduced to the scientific world about the beginning of the present century; it is a close relative of such familiar North American weeds as boneset, Joe-Pye-weed, and the plant that causes occasional outbreaks of milk sickness in the Midwest. After its discovery by Europeans it rapidly acquired the name of "the sweetest plant in the world." A very small piece sufficed to sweeten a cup of coffee or tea.

During the past generation several partially successful attempts have been made to isolate and study the particular substance in the plant that made it so intensely sweet. It has remained, however, for the French chemists, MM. Briddel and Lavielle, to accomplish the final purification.

They have discovered, to their surprise, that the sweet crystals of stevioside, upon chemical treatment to remove a part of the combined water in them, break apart into about 60 per cent. common glucose and 40 per cent. of a new stuff which they called "steviol." The latter has no taste, but combined with the glucose it produces a most poignantly sweet substance.

MM. Briddel and Lavielle made another interesting discovery, the significance of which is not yet clear. If they freeze a 50 per cent. solution of the intensely sweet stevioside they obtain a mat of fine needle-crystals, which contain more chemically combined water than the original substance, and which are only faintly sweet. The sweetness of stevioside seems to depend on the presence of an exact amount of water in combination with the glucose and steviol; a trifle more or a trifle less spoils the effect.—(*Science Service.*)

BOOK REVIEWS

PLANT-MICROCHEMISTRY. By Tunmann-Rosenthaler. 2d enlarged ed., 1047 pp., 190 text-figures. Marks 78, bound. Borntraeger, Berlin. 1931. (In German.)

Here we have a book of real aid in the interesting microchemical study of plant objects. In the general part (I) we find a helpful discussion of microtechnical operations, or reagents, methods, optical data; in the special section (II) the inorganic substances, the organic compounds; in (III) the protoplast-plasma and contents; in (IV) the cell membranes are discussed. Newly introduced are the descriptions of the manipulator, of microtechnical methods, of ordinary and vital staining methods, of microchemical characteristics of bacteria and fungi and of many new compounds. Numerous references will assist the worker in finding the original contributions to literature, although the details given make that need likely often unnecessary.

Tunmann conceived plant microchemistry as an indispensable tool for botanists, pharmacognocists, pharmacists, food and plant chemists and all who study plant objects. Rosenthaler certainly was well qualified to continue and elaborate on Tunmann's work. While microchemical methods and results, observed in plant tissue, often necessitate the verification of findings outside the plant; while furthermore the identification of some substances, as membrane substances, is made difficult, certain advantages often stand out: 1. The economy of material; 2. The localization of the valuable substance; 3. The ease and quickness of the procedure; 4. The conclusiveness of the result.

Those who depend on microchemical data for purposes of researches in plant life, and also for the identification and evaluation of foods and drugs, of technical raw materials and other plant products, will hail this comprehensive book as a welcome if not indispensable guide.

ARNO VIEHOEVER.

PRINCIPLES OF MODERN PERFUMERY. By Alfons M. Burger. ca. 200 pp., 5 text illustrations. Marks 8.50, unbound. W. de Gruyter & Co., Berlin-Leipzig. 1930.

Much, the author claims, has been accomplished in the last ten years. The preparation of various natural products as flower oils and resinoids has been much improved; by means of advanced knowledge of organic chemistry a large number of new synthetic perfume substances, embodying new odor combinations, has been created; it has become possible to prepare certain valuable natural, plant, and animal perfumes in the laboratory. Thus the working scope of the perfume manufacturer has been greatly increased and enables him to present in modern perfumery his art, based on much experience and knowledge of the new possibilities to combine, like the composer of new tone combinations, new perfume combinations with a personal touch, an original fragrance.

A few practical hints, suggesting the use of certain microchemical means, are given for the recognition, control and analysis of the perfume. Then follows a description of the basic perfumes—the natural and the synthetic; and finally of the combined perfumes (specialties). In the special part is a discussion of the preparation of different perfume types and of graphic formulæ (using horizontal lines in such lengths as to indicate the amounts of substances in the formula, the names of the components are placed on a vertical line from which all horizontal lines start; the measure of length is indicated by a graduated horizontal head and bottom line.

The subject of fixing and supporting the perfume by means of crystalline perfumes as vanillin and cumarin, by resinoids and purified extracts of drugs or plants, is then mentioned and followed by a detailed discussion with graphic formulæ of special types, including the modern phantasy perfumes. A list of thirty-six perfume factories in European countries, as France, Germany, Holland, Switzerland and Italy, is given, as well as a solubility table of seventy-six most used chemical perfumes in dilute alcohol of stated concentrations. The author aims with his book to place perfumery on a higher level and it appears that he has remarkably well succeeded—an interesting survey from an expert, informed, informing.

ARNO VIEHOEVER.

HANDBOOK OF PHARMACOGNOSY, 2d enlarged ed., vol. 1, sec. 2, by A. Tschirch in co-operation with fifteen authors. B. Tauchnitz, Leipzig, 1931. Each issue of 111 pages, 8 marks subscription price. (In German.)

Three new issues (6, 7, 8) have recently been published, with 125 illustrations, discussing in the thorough manner, formerly mentioned in connection with a review of the first section, now the botanical, zoological and (in part) the chemical phases of pharmacognosy. Thus, under pharmaco-botany we have—

1. Pharmaco-taxonomy: botanical gardens, herbaria, terminology, floræ and illustrations;
2. Pharmaco-morphology: drug collections, descriptions and terminology;
3. Pharmaco-anatomy: micro-chemistry, micro-sublimation, micro-polarization, microscopic technic, measurements, development, anatomical charts, permanent preparations;
4. Pharmaco-physiology: the biology of drugs and drug constituents—and fermentation;
5. Pharmaco-cytology and genetics: importance of chromosomes, the selection and breeding;
6. Pharmaco-pathology: organisms (plant and animal) harmful to medicinal plants and drugs.

Under Pharmaco-zoology we find an enumeration of mainly historical interest, namely—

1. Human tissues, excreta, etc., used as drugs (20);
2. Whole animals, used as drugs (70);
3. Animal organs, used as drugs (201);
4. Animal secretions and excretions, used as drugs (46);
5. Abnormal animal structures, used as drugs (14);
6. Fossil animal parts, used as drugs (7);
7. Strange bodies, used as drugs (8).

Under Pharmaco-chemistry we find a discussion of the object, the methods and a general survey of drug constituents as polysaccharides, glucosides, pigments, tannins, resins.

Much of this diversified information collected should reach both teacher and student to increase the interest in a subject, here so fasci-

natingly treated, to broaden the outlook of its usefulness, and to lead either to the immediate application of new knowledge or to the solution of still unsolved problems. It is a record full of experiences, full of suggestions.

ARNO VIEHOEVER.

QUININE, in general medical practice—with consideration of pharmacological observations. By Dr. Med. Fritz Johannessohn. 232 pages, 3 illustrations. 1930. Published by the Bureau for the Increased Use of Quinine, Amsterdam, Holland.

There are eight chapters on Quinine, with a reference list of 652 literature references; one on Quinidine, with a list of 157 references to literature. In the introduction mention is made of Gomes, who in 1810 isolated the cinchonine in crystals; and Profs. Caventou and Pelletier, connected with the pharmaceutical faculty of the University of Paris, who isolated pure strychnine in 1818 and quinine in 1820; their pictures are prominently placed next to the inside front cover. Quinine, after having been almost exclusively used against fever, until the properties of salicylic acid, antipyrin and aspirin were discovered, has now found a use in internal medicine: pneumonia, influenza, heart troubles, and migraine; in obstetrics, and in surgery.

In the second chapter are discussed occurrence and methods of production—the old one still practiced in South America and the newer and most prevalent methods used in Java and the East Indies. In the third chapter the chemistry of quinine is mentioned and a considerable number of identification tests are given. In the fourth chapter the distribution and precipitation of quinine in the system are treated. The fifth chapter deals with the therapeutic application, the disinfectant effect on germs, the stimulating effect on organs, muscles and nerves. In the sixth chapter, dealing with diagnosis, the change of resistance of the red blood corpuscles to hemolysis by quinine is perceptible in diseases as diabetes, kidney and infections. The seventh chapter refers to peculiar effects (idiosyncrasy) of quinine on some people, and the eighth chapter mentions forms of applying quinine so as to hide the taste: for children, the administration of the almost tasteless quinine tannate, or certain esters of quinine; black coffee or some drops of tincture of eryodictyon are said to remove the bitter taste from the mouth, when none of the newer gelatine quinine cap-

sules or other tasteless forms of administration are available. A warning is also given that quinine should not be compounded with aspirin, causing a transformation to chinotoxin or alkaloid precipitants as they form incompatible mixtures.

A brief chapter is included dealing with quinidine, the stereo isomer of quinine, and its main use in heart troubles, especially as a preventive in fibrillations of the auricles.

This is a remarkably thorough, and, as far as we can see, unbiased, up-to-date treatise on one of our most valued drugs. It could well serve as a model for other monographs on drugs and their active constituents.

ARNO VIEHOEVER.